REMARKS

Status of the Claims

Claims 21-27 are pending. Claims 21-27 are rejected.

The 35 U.S.C. §112, first paragraph rejections

Claims 21-27 are rejected under 35 U.S.C. §112, first paragraph, as lacking enablement because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant respectfully traverses the rejection.

The Examiner states that the specification confines its teachings to methods of predicting an increased risk for prostate cancer by comparing the concentration of IGF-I to a reference level, wherein an elevation of at least 100 ng/ml above the reference level indicates a doubling of the risk for prostate cancer. The claims are drawn to methods where even a small increase in IGF-I concentration above a reference level indicates an increased risk for prostate cancer; but it is not clear from the specification what IGF-I elevations are significant, and how elevations less than 100 ng/ml correlate to any risk for prostate cancer. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant respectfully traverses the Examiner's rejection. The specification teaches that there is a significant association between having an IGF-I level above the

reference level and risk of prostate cancer. The reference category is shown in Table I as the first quartile of the control group; the reference level then refers to the upper end of the IGF-I range in this group. According to the data presented in Table 2 as an analysis of the data in Table I, there is shown a significant linear trend between increased circulating IGF-I levels and increased risk of prostate cancer when the incidence of prostate cancer occurring in test subjects within quartiles 2-4 are compared to the incidence of prostate cancer in the reference range (see page 9, lines 22-24 and page 11, lines 6-11). The linear trend was such that after adjusting for IGFBP-3, a 100 ng/ml increase in IGF-I corresponded to an approximate doubling of relative risk when compared to the reference level (see page 11, lines 6-11 and Table 2). The doubling of risk for a 100 ng/ml elevation of IGF-I is described as a particular point in the linear trend; however, elevations below 100 ng/ml would also correspond to a significant increased risk for prostate cancer, being part of the same linear trend. Because the specification defines the reference level and demonstrates a significant increase in the risk of prostate cancer for IGF-I levels that are above the reference level, Applicant respectfully submits that one skilled in the art would not be required to engage in undue experimentation to practice the invention as claimed. Accordingly, Applicant respectfully requests that the rejection under 35 USC 112, first paragraph, be withdrawn.

The 35 U.S.C. §102(b) rejections

Claims 21-27 are rejected under 35 USC 102(a) as being anticipated by **Mantzouros** (Mantzouros *et al., British Journal of Cancer* 76(9): 1115-1118, 1997). Applicant respectfully traverses the rejection.

The Examiner states that **Mantzouros** teaches a method of predicting risk of prostate cancer where concentrations of IGF-I are measured in healthy individuals and where IGF-I concentrations are measured in test individuals that have either prostate cancer or BPH, and where a risk of prostate cancer is determined by comparing IGF-I levels to a reference. **Mantzouros** teaches that an increase in IGF-I in 60 ng/ml leads to a 91 percent increase in risk of prostate cancer; therefore, **Mantzouros** teaches methods that are the same as those claimed.

Applicant respectfully traverses the Examiner's rejection. In **Mantzouros**, blood samples were collected from individuals with histologically confirmed cases of prostate cancer or BPH, and from healthy individuals as controls (see Abstract). The levels of IGF-I were compared between the cases and controls and found to be overall elevated in the prostate cancer cases; **Mantzouros** found that an increase of 60 ng/ml corresponded to an odds ratio of 1.91, indicating an increased risk of prostate cancer (see *Id.*). **Mantzouros** therefore determined an increased risk of prostate cancer from comparing samples from individuals already having prostate cancer with samples from healthy individuals (see Abstract and Table 1). In contrast, the present specification describes a study in which all individuals, both the cases and the controls, were healthy at the time of sample collection; all assays reported for the cases are from blood specimens collected an average of seven years prior to clinical diagnosis of prostate cancer (see page 8, lines 16-17). Therefore, the study described in the present specification is prospective, whereas the **Mantzouros** study was retrospective. In addition, unlike the teachings of the present specification, because of its retrospective nature the **Mantzouros** study could not rule out

possible effects of the cancer itself, or cancer treatment, on IGF-I levels (see the paragraph spanning pages 14-15).

The claims as currently amended recite measuring the concentration of IGF-I in a body fluid from a healthy individual outside the reference group, and comparing the concentration of IGF-I in the healthy individual outside the reference group to the reference level, wherein an elevated concentration of IGF-I above the reference level indicates an increased risk for prostate cancer. In contrast, **Mantzouros** teaches the measurement of IGF-I concentrations in test individuals that have either prostate cancer or BPH at the time of such measurement, and where a risk of prostate cancer is determined by comparing IGF-I levels to a reference. Applicant therefore respectfully contends that because the methods in the claims as currently amended are not the same as those taught in **Mantzouros**, the present claims are not anticipated by **Mantzouros**. Accordingly, Applicant respectfully requests that the rejection under 35 USC 102(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed March 28, 2006. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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